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UPDATE ON CONTRACEPTION (2): USE IN SPECIFIC POPULATIONS

- **Women should be informed that oral emergency contraceptives delay ovulation, however ovulation may still occur in the same cycle; there may be a risk of pregnancy from future unprotected sexual intercourse in that cycle**
- **Drug interactions should always be considered when prescribing hormonal contraceptives due to the potential risk of contraceptive failure or other adverse effects**
- **Progestogen-only contraceptives are the hormonal contraceptives of choice in breastfeeding women**
- **The UK Faculty of Sexual and Reproductive Healthcare (FSRH) website has a number of useful guidance documents on contraception for specific populations**

INTRODUCTION

The choice of a contraceptive method depends on the effectiveness of the method and the individual patient, with consideration of factors such as age, co-morbidities, concomitant medications and preferences of the user.[1,2] The UK Faculty of Sexual and Reproductive Healthcare (FSRH) has guidance documents covering many of these aspects. **Most women will need to use contraception for >30 years and the method of contraception may change with time.**[3] Table 1 outlines factors to consider and to discuss with a patient when deciding on contraception.

Table 1: Factors to consider when choosing contraception[3]

- The patient's medical history including relevant family, menstrual, contraceptive and sexual history
- The patient's medical eligibility for the various contraceptive options and a discussion of the risks and benefits of those options
- Any issues that might affect the patient's choice of contraception
- Exclusion of pregnancy by taking menstrual and sexual history
- Women requesting CHC should be informed about the effectiveness (of both typical and perfect use) of CHC, and of the superior effectiveness of LARC
- Assessment for risk of sexually transmitted infections and testing where appropriate
- Promotion of safer sex

CHC-combined hormonal contraception; LARC-long-acting reversible contraception

Women requesting contraception should be informed about the effectiveness (of both typical and perfect use) of the various contraceptive methods. Table 2 outlines the failure rates associated with both "perfect" and "typical" use of contraceptive methods.

Table 2: Percentage of women experiencing an unintended pregnancy within the first year[4]

Method	Typical use (%)	Perfect use (%)
No method	85	85
Female condom	21	5
Male condom	18	2
Combined hormonal contraception*	9	0.3
Progestogen-only pill	9	0.3
Progestogen-only injectable	6	0.2
Copper intrauterine device	0.8	0.6
Levonorgestrel intrauterine system	0.2	0.2
Progestogen-only implant	0.05	0.05

*includes combined oral contraception, transdermal patch and vaginal ring

This, the second bulletin on contraception, will review the use of contraception in some specific populations and highlight useful resources on contraception.

EMERGENCY CONTRACEPTION

Emergency contraception (EC) is a method of preventing unintended pregnancy following unprotected sexual intercourse (UPSI).[5-7] Table 3 summarises the various types of EC (i.e. copper intrauterine device [Cu-IUD], oral levonorgestrel [LNG] and ulipristal acetate [UPA]) currently available in Ireland.

The most effective method of EC is the Cu-IUD, which is the only method of EC that is effective after ovulation has taken place;[5,6] the failure rate is reported to be 1:1000.[5] Oral EC delays ovulation and should be taken as soon as possible after UPSI.[6] Of the two types of oral EC options, evidence suggests that UPA is more effective than LNG from 0 to 120 hours after UPSI.[5,6,10] The efficacy of oral EC may be affected by body weight (see section on obesity).

Adverse effects associated with EC include pain with Cu-IUD insertion, and headache, nausea, abdominal pain and altered bleeding patterns with LNG or UPA.[6,8,9] Women should be advised to seek medical advice if vomiting occurs within 3 hours of taking EC; a repeat dose of the same method or a Cu-IUD may be offered if appropriate.[6] Altered bleeding may occur after oral EC; a pregnancy test should be carried out if menses are delayed by more than 7 days.[6]

Special considerations: The effectiveness of UPA-EC could be reduced if a woman takes any progestogen in the 5 days after taking UPA-EC, and could theoretically be reduced if a woman has taken a progestogen within 7 days prior to taking UPA-EC.[6] Note that if a woman has already taken UPA-EC, LNG-EC should not be taken in the following 5 days, and if the woman has already taken LNG-EC, UPA-EC could be less effective if taken in the following 7 days.[6]

Enzyme-inducing drugs (EIDs) have the potential to reduce the contraceptive efficacy of LNG and UPA; the Cu-IUD is the only method of EC not affected by EIDs.[5,6] Women taking EIDs who are not suitable for a Cu-IUD should be advised to take 3 mg LNG (unauthorised use).[5,6]

Table 3: Methods of emergency contraception in Ireland[5,6,8,9]

Type of emergency contraception (Mode of action)	Recommended use	Undesirable effects include*:
Copper intrauterine device (Cu-IUD) (non-hormonal) (Primarily by inhibiting fertilisation; if fertilisation has occurred there is an anti-implantation effect)	Use within the first 120 hours following first UPSI in a cycle or within 5 days from the earliest estimated date of ovulation IUD retained until pregnancy excluded (e.g. onset of next menstrual period) or for licensed duration of IUD	Pain on insertion – analgesia recommended
Levonorgestrel (LNG) 1.5 mg single oral dose (Primarily by inhibiting ovulation and may delay ovulation)	Licensed for use within 72 hours of UPSI or contraceptive failure	Nausea, abdominal pain, heavy menses (very common); cases of VTE reported Reduced efficacy with enzyme-inducing drugs and potential DDI with ulipristal acetate – concomitant use not recommended
Ulipristal acetate (UPA) 30 mg single oral dose (Progesterone receptor modulator – delays ovulation)	Licensed for use within 120 hours of UPSI or contraceptive failure	Vomiting, abdominal pain (common) Not recommended in severe asthma treated with oral steroids Reduced efficacy with enzyme-inducing drugs; potential DDI with progestogens - additional contraceptive precautions required

* - refer to Summary of Product Characteristics for full prescribing information; UPSI – unprotected sexual intercourse, IUD – intrauterine device, VTE – venous thromboembolism, DDI – drug-drug interaction

It is important that women are aware that oral ECs delay ovulation, however ovulation may still occur in the same cycle and that they may be at risk of pregnancy from future UPSI in that cycle.[5,6] Advice on the initiation or continuation of regular contraception and on the required additional contraceptive precautions differs depending on the type of EC used and the method of contraception. **Note that women who have taken UPA-EC should delay the start of any progestogen-containing contraceptive method for 5 days taking additional contraceptive precautions during this time.**[1,5] Women who start hormonal contraception after EC should have a pregnancy test 21 days after the last episode of UPSI.[6]

WOMEN ON CONCOMITANT MEDICATIONS: DRUG INTERACTIONS

Drug interactions should always be considered when prescribing hormonal contraceptives, due to the potential risk of contraceptive failure or other adverse effects.[1,11] Women should be informed that some medicines may interact with hormonal contraceptives and advised not to start medicines (including over-the-counter medicines) without checking with a healthcare professional (HCP).

Impact of medicines on contraceptive hormones: Concomitant drugs may alter the serum levels of contraceptive hormones; see table 4 for some examples (this list is not exhaustive).

The effectiveness of some hormonal contraceptive methods including combined hormonal contraceptives (CHCs), progestogen-only pills (POPs) and the etonogestrel implant (ENG-IMP), may be reduced with co-administration of enzyme-inducing drugs (EIDs) and for 28 days after stopping them.[1,11,13,14] **Women using EIDs should be advised to use a contraceptive method that is not affected by EIDs such as the Cu-IUD, levonorgestrel intrauterine system (LNG-IUS) or depot medroxyprogesterone acetate (DMPA).**[11,14] Griseofulvin is not an EID, however it also reduces the efficacy of some hormonal contraceptives.[5,11,17] **The use of CHCs, POPs and ENG-IMP should be avoided in women taking EIDs**[1,5,11,13-16] **or griseofulvin.**[5,11,17] The use of short-term EIDs can be managed more flexibly than longer term EID use.[1,11] Women who have been advised to switch methods may still wish to choose the COC; if necessary to use COC concomitantly with an EID (with the exception of rifampicin or rifabutin), a minimum of 50 microgram (30 microgram and 20 microgram) ethinylestradiol (EE) monophasic combined pill (unauthorised use) may be considered during use of an EID and for 28 days after stopping.[1] A continuous or tricycling regimen plus a shortened pill-free interval of 4 days should be used if this higher EE dose strategy is chosen.[1,11] Breakthrough bleeding could indicate low serum EE concentrations.[1]

Note that for **women taking COCs, the use of most broad spectrum antibiotics that are not enzyme-inducing does not require any precautions, unless the antibiotic (and/or illness) causes vomiting or diarrhoea.**[5,11] Women should be advised to follow the missed pill instructions if vomiting occurs within 3 hours of taking COC or if severe diarrhoea occurs for >24 hours.[1]

Table 4: Drugs affecting the metabolism of hormonal contraception[11,12]

Stages of metabolism: drug interactions/effects	Types of drugs
Absorption May be affected by drugs that cause vomiting or severe diarrhoea, chelating drugs and drugs that alter gastric pH or gut transit	Drugs that increase gastric pH (e.g. PPIs and antacids) may reduce absorption and efficacy of UPA Drugs that induce diarrhoea or vomiting
Metabolism Induction of CYP-450 enzymes may reduce hormones resulting in decreased contraceptive efficacy	**Enzyme-inducing drugs that may decrease efficacy** include antiepileptics (e.g. carbamazepine, topiramate), antibacterials (e.g. rifabutin, rifampicin), antiretrovirals (e.g. efavirenz), St John's wort, modafinil
Inhibition of CYP-450 enzymes may increase hormone levels potentially resulting in increased adverse effects	**Enzyme-inhibiting drugs that may increase hormone levels** include antibacterials (e.g. erythromycin), antifungals, antiretrovirals (e.g. atazanavir), immunosuppressants, NSAIDs, statins

PPIs - proton pump inhibitors; UPA - ulipristal acetate; CYP 450 - Cytochrome P450; NSAIDs - non-steroidal anti-inflammatory drugs

Impact of contraceptive hormones on other medicines: There are certain medicines whose plasma levels may be altered (reduced or increased) by hormonal contraceptives.[11]

Hormonal contraceptives that may reduce the effects of medicines: CHCs may reduce lamotrigine exposure, which could potentially result in reduced seizure control while using CHC, and then subsequent increased lamotrigine levels (in the hormone-free interval) with a potential increased risk of lamotrigine toxicity; an alternative contraceptive method should be considered.[1,11] UPA-EC may reduce the effectiveness of LNG-EC and possibly other hormonal contraceptives.[11] Estrogens may also antagonise the effects of

antihypertensive and antidiabetic agents and may increase the requirements for thyroid hormones in hypothyroidism.[11]

Hormonal contraceptives that may increase the effects of medicines: Hormones such as EE may increase the levels of some immunosuppressants (e.g. tacrolimus and ciclosporin) and monitoring may be required.[11] Some evidence suggests that desogestrel may increase lamotrigine levels and adverse effects.[11,17] Other medicines whose plasma levels may be increased when co-administered with hormonal contraceptives include voriconazole, chlordiazepoxide, diazepam, theophylline and tizanidine.[11] Additive hyperkalaemia may occur with co-administration of drospirenone and potassium-sparing diuretics.[5,11]

The FSRH has a useful guide on drug interactions.[11] There is a potential for many drug interactions between contraceptive hormones and antiretroviral therapies; the HIV Drug Interaction Checker is a useful resource (see useful sources).

CONTRACEPTION FOR BREASTFEEDING WOMEN

Contraception, when required, should be initiated by 21 days after birth.[18] Women who 1) are less than 6 months postpartum, 2) are fully breastfeeding and 3) remain amenorrhoeic (otherwise known as criteria for the lactational amenorrhoea method [LAM]) have a 2% risk of conception;[5,12] this compares well with other contraceptive methods.[12] **To avoid an unintended pregnancy, contraception is required from 21 days postpartum, if all three criteria for LAM are not fully met.[6,12]**

Progestogen-only contraception (including LNG-IUS, ENG-IMP, DMPA and POP) are not associated with adverse breastfeeding outcomes or adverse effects for infants of breastfeeding women;[12,18-22] they are the hormonal contraceptives of choice in medically eligible (see bulletin 1) breastfeeding women.[12,18-22] **The POP, which is considered to be nearly 100% effective in breastfeeding women, is often considered a first choice.[12]**

The Cu-IUD, which does not have a significant effect on breastfeeding or infant growth, can be used in breastfeeding women.[18,20] Insertion of intrauterine contraceptives (IUCs) (both LNG-IUS and Cu-IUD) should take place within 48 hours after delivery or after 28 days postpartum.[18,20] There is an increased risk of uterine perforation with IUCs (both LNG-IUS and Cu-IUD), which while rare, is reported to be up to 6 to 10 times higher in breastfeeding women.[23] The initiation of IUC or progestogen-only contraception is safe immediately after delivery (even though contraception is not required until 21 days after birth) and is associated with a reduced risk of unplanned pregnancy.[18]

Combined hormonal contraception (CHC): There is limited evidence on the use of CHC in breastfeeding women; this use is outside the product licence.[18] Evidence about the impact of CHCs on breastfeeding is inconsistent;[20,24,25] limited evidence suggests that CHC does not adversely affect infant outcomes with later initiation (some cases of transient gynaecomastia reported).[20,21,24] **CHCs are associated with an increased risk of venous thromboembolism (VTE), and all women should undergo a risk assessment for VTE postnatally.[18]** Guidance on the use of CHC in breastfeeding women is also conflicting. The FSRH advises that women who are medically eligible (and without additional risk factors for VTE) can use CHC six weeks after delivery;[18] the WHO and other sources recommend waiting six months.[20,22,24] However, it has been suggested that CHC should not be used in breastfeeding women as POPs are so effective in this population.[12]

Emergency contraception (EC) in breastfeeding women: EC is recommended for breastfeeding women who have had UPSI, from 21 days after delivery, if any of the 3 LAM criteria mentioned above are missed.[6,18] There are no specific safety concerns with use of LNG or UPA in breastfeeding women.[18] No adverse effects have been observed in infants exposed to LNG in breastmilk,[21] however there is little evidence on the use of UPA in breastfeeding.[20] UPA is not the preferred EC for breastfeeding women; some sources advise that women should not breastfeed for 7 days after taking UPA.[6,9,18] A Cu-IUD, which is the most effective EC can be used from 28 days postpartum in breastfeeding women;[6,18,20] it can be inserted up to 120 hours after UPSI and can also be used to provide long-term contraception.[26]

OBESITY AND CONTRACEPTION

There is an increasing prevalence of obesity (body mass index [BMI] ≥30 kg/m^2) worldwide.[27] **It is important that all women including those with high BMIs have access to effective and safe contraception.[27]** Women with obesity are at increased risk of other co-morbidities (e.g. VTE, hypertension, dyslipidaemias, type 2 diabetes, cardiovascular disease [CVD], stroke, and some cancers) compared with women with a normal BMI, and these aspects need to be considered when providing contraception.[27] **It is of note that the baseline risk for VTE in obese women is two-fold higher than the VTE risk in normal weight women.[27]** There is limited data on the use of hormonal contraceptives in women who are overweight or those with obesity; many of the studies are observational studies, which are subject to confounding factors.[27]

Intrauterine contraception: Evidence suggests that the efficacy of Cu-IUDs and LNG-IUSs are not affected by body weight or BMI.[27] The available evidence suggests that IUC is a safe contraceptive option for women who are overweight and for women with obesity.[27] While IUC insertion may be more challenging in women with obesity than in women of normal weight, raised BMI is not a significant factor in failed IUC insertions or expulsions.[27]

Progestogen-only implants: The Summary of Product Characteristics (SmPC) of Implanon NXT® advises that the contraceptive effect of ENG-IMP is related to the plasma level of etonogestrel, which is inversely related to body weight, and which decreases with time after insertion.[28] It states that it cannot be excluded that the contraceptive effect in heavier women may be less than in women of normal weight and that healthcare professionals may consider earlier replacement of the implant in heavier women.[28] The FSRH, however, advises that the current available evidence is reassuring and that there is no direct evidence to support a need for earlier replacement of ENG-IMP.[27] Another source recommends that a discussion regarding earlier replacement of ENG-IMP with young fertile women >100 kg weight is reasonable, especially if she has also begun to cycle regularly in the third year.[5]

Progestogen-only injection: The overall data suggests that weight or BMI do not impact on the effectiveness of DMPA.[27] **The use of DMPA in women with obesity who have other risk factors for CVD (e.g. smoking, diabetes and hypertension) is considered UKMEC 3 (i.e. the risks usually outweigh the benefits of using**

this method).[27] The data on whether there is an association between DMPA and VTE is inconclusive.[27] Evidence suggests that the use of DMPA is associated with weight gain.[27] The use of a longer needle or deltoid administration can be considered when administering DMPA in women with obesity.[27]

Progestogen-only pill: There is conflicting advice on the use of POP in women with raised BMI. The FSRH advises that the available evidence does not show an increased risk of pregnancy in POP users with a heavier weight or a higher BMI;[13,27,29] double-dose POP is not recommended.[27] One source advises that women >100 kg should take 2 doses of the POP desogestrel (unlicensed use).[5,12]

While there is no data on the safety of progestogen-only contraceptives in obese women, the limited safety data is reassuring.[27]

Combined hormonal contraceptives: The findings of studies of the effectiveness of combined oral contraceptives (COC) in relation to increased body weight or BMI vary.[27] Overall, most evidence (from high quality studies) suggests that there is no association between weight or BMI and the effectiveness of COC.[1,27,30-33] There is limited evidence that suggests a possible reduction in the effectiveness of the contraceptive patch in women ≥90 kg, therefore an alternative method or additional precautions should be advised for women ≥90 kg.[1,27,32-34] Limited evidence suggests that the effectiveness of the contraceptive ring is not affected by weight.[27] **In terms of safety, the use of CHC is considered UKMEC 3 for women with a BMI of ≥ 35 kg/m^2 (i.e. the risks generally outweigh the benefits)**; this is due to the additive risk of VTE from obesity and use of CHC.[27]

There is some evidence that there is a potential for reduced effectiveness of oral contraceptives (i.e. COC and POP) for women who have had bariatric surgery;[1,27,35] an alternative contraceptive method should be considered.[1,27,35]

Emergency contraception: The evidence suggests that there may be reduced efficacy of hormonal EC with increased body weight especially LNG-EC.[5,6,27,36-39] **The FSRH recommends that if a Cu-IUD is not suitable in women weighing >70 kg or with a BMI >26 kg/m^2, such women can be offered UPA-EC, or if UPA-EC is not suitable, a double dose of LNG-EC (3 mg) can be used (unauthorised).[6]**

CONTRACEPTIVE ADVICE FOR WOMEN ON POTENTIALLY TERATOGENIC DRUGS

It is important that women who are taking (or whose partners are taking) known or potentially teratogenic drugs are on an effective form of contraception. In utero exposure to some drugs (e.g. retinoids, methotrexate and valproate) is associated with a very high risk of devastating birth defects, and these women in particular need a highly effective form of contraception.[5,11] While no method of contraception is 100% effective,[40] **contraceptive methods that are considered "highly effective" include the long-acting reversible contraceptives (LARC) (Cu-IUD, LNG-IUS and ENG-IMP) and male or female sterilisation.[5,40]** Women should be advised that these contraceptive methods have a failure rate of <1% with typical use.[40] Note that there may be reduced contraceptive effectiveness in women using ENG-IMP in combination with EIDs, therefore EIDs should be avoided and/or an alternative highly effective contraceptive method used instead.[5,40] **Women should be advised that the typical use failure rate is 9% for CHCs, 9% for the POP and 6% for DMPA** (see table 2).[40] Women on known or potentially teratogenic drugs who use these contraceptive methods should be advised to use additional contraceptive precautions (e.g. condoms) and should also be advised not to take any interacting drugs that could reduce contraceptive effectiveness. **The use of barrier methods, withdrawal and fertility awareness methods alone is not recommended.[40]**

CONTRACEPTION FOR OTHER SPECIFIC POPULATIONS

As discussed earlier, most women will need to use contraception for >30 years and the method of contraception required may change with time. The FSRH has a number of useful guidance documents on contraception for specific populations including:

- Contraception after pregnancy
- Overweight, obesity and contraception
- Contraceptive choices for young people
- Contraception for women aged >40 years
- Contraceptive choices for women with cardiac disease
- Sexual and reproductive health for individuals with inflammatory bowel disease
- Contraceptive choices and sexual health for transgender and non-binary people

Useful Resources:

- The NMIC clinical enquiry answering service is available for prescribers on all aspects of contraceptive use: nmic@stjames.ie
- The UK Faculty of Sexual and Reproductive Healthcare provides useful guidance for healthcare professionals on contraceptive methods: http://www.fsrh.org/
- Contraception Today, John Guillebaud, CRC Press
- Contraception: Your Questions Answered, John Guillebaud and Anne MacGregor, Elsevier
- Stockley's Drug Interactions: www.medicinescomplete.com (subscription required)
- HIV Drug Interaction Checker: www.hiv-druginteractions.org
- "Think Contraception": A useful website for the general public on contraceptive issues (including age specific guidance): http://www.thinkcontraception.ie/

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